Survival of European adolescents and young adults diagnosed with cancer in 2000–07: population-based data from EUROCARE-5

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Summary

Background

Data from EUROCARE have consistently shown lower survival for adolescents and young adults (AYAs; aged 15–24 years) than for children (0–14 years) for most cancers that affect both groups, and modest survival improvements up to 2000–02. AYAs have longer survival than that of adults for most cancers. We used the latest definition of AYAs (aged 15–39 years) and provided estimates of 5-year relative survival for European AYAs with cancer diagnosed in 2000–07, compared with children and adults (40–69 years) with cancer, and assessed survival improvements over time.

Methods

We analysed data from population-based cancer registries of 27 European countries participating in EUROCARE-5. We used the so-called complete method to estimate 5-year, population-weighted relative survival for 19 cancers affecting AYAs and children, and for 27 cancers affecting AYAs and adults. We assessed relative-survival differences between children versus AYAs, and between AYAs versus adults, using the *Z* test. We used the period approach to estimate 5-year relative survival over time for children and AYAs, and used a generalised linear model to model survival time trends (1999–2007) and to assess the significance of changes over time.

Findings

We analysed 56 505 cancer diagnoses in children, 312 483 in AYAs, and 3 567 383 in adults. For all cancers combined, survival improved over time for AYAs (from 79% [95% CI 78·1–80·5] in 1999–2002 to 82% [81·1–83·3] in 2005–07; p<0·0001) and children (from 76% [74·7–77·1] to 79% [77·2–79·4]; p<0·0001). Survival improved significantly in children and AYAs for acute lymphoid leukaemia (p<0·0001) and non-Hodgkin lymphoma (p<0·0001 in AYAs and p=0·023 in children). Survival improved significantly in AYAs only for CNS tumours (p=0·0046), astrocytomas (p=0·040), and malignant melanomas (p<0·0001). Survival remained significantly worse in AYAs than in children for eight important cancers: acute lymphoid leukaemias, acute myeloid leukaemias, Hodgkin's lymphomas, non-Hodgkin lymphomas, astrocytomas, Ewing's sarcomas, and rhabdomyosarcomas (p<0·0001 in all cases), and osteosarcomas (p=0·011).

Interpretation

Notwithstanding the encouraging results for some cancers, and overall, we showed poorer survival in AYAs than in children for the eight important cancers. Recent European initiatives to improve

outcomes in AYAs might reduce the survival gap between children and AYAs, but this reduction can only be verified by future population-based studies.

Funding

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Introduction

No internationally agreed definition exists for adolescents and young adults (AYAs) for cancer purposes; age ranges of 15–24 years and 15–29 years (at cancer diagnosis) have been used. EUROCARE[1] has shown that AYAs (aged 15–24 years) have poorer survival than children (aged 0–14 years) for most cancers that affect both groups, and survival improvements up to 2000–02 were modest. Additionally, AYAs (aged 15–29 years) have better survival than adults for most cancers.[2] Poorer survival in AYAs than in children has been attributed to various factors including no or few clinical trials conducted in AYAs, the dearth of specific treatment guidelines, differences in cancer biology, variations in the pharmacokinetics of chemotherapeutic agents, and delays in diagnosis and treatment.3, 4, 5, 6, 7 AYAs with cancer are, in many ways, neglected by both paediatric and adult oncologists, yet effective disease management necessitates a multiprofessional approach incorporating expertise from both specialties.[8] To improve cancer outcomes for AYAs, various initiatives—including promoting collaboration between paediatric and adult oncologists, developing national policies for managing AYAs with cancer, and setting up specific treatment units—have been implemented in several European countries[8] and worldwide.[9]

In the present EUROCARE-5 study, we used the latest definition of AYAs (age 15–39 years) proposed by the US National Cancer Institute[10] and accepted by the European Network for Cancer in Children and Adolescents (ENCCA) to provide population-based analyses of 5-year relative survival for European AYAs with cancer, compared with survival in children (aged 0–14 years) and adults (aged 40–69 years). We also present time trends in 5-year relative survival for cancers typically occurring in AYAs and children, to assess whether survival improvements in the older age group still lag behind those in children. The time period of our analyses pre-dates implementation of the European initiatives to improve outcomes for AYAs, and thus provides an important baseline from which to assess the effectiveness of these initiatives.

Research in context

Evidence before this study

There is no internationally agreed definition of adolescents and young adults (AYAs) for cancer purposes; age ranges of 15–24 years and 15–29 years (at cancer diagnosis) have been used. The US National Cancer Institute proposed defining AYAs as those aged 15–39 years at diagnosis. The European Network for Cancer in Children and Adolescents has adopted this definition and is promoting its use in Europe. Less is known about factors that affect cancer incidence, outcomes, and quality of life in AYAs than other age groups. Furthermore AYAs with cancer have not had the same mortality reduction seen in recent years in younger and older patients with cancer (for some cancers). To try to improve outcomes for AYAs with cancer, various initiatives—including the promotion of collaboration between paediatric and adult oncologists, development of national policies for managing AYAs with cancer, and setting up of AYA-specific treatment units—have been implemented in several European countries. Over the past 5 years population-based analyses of incidence and outcomes for AYAs with cancer have been completed in France, the Netherlands,

and the UK. However, the latest survival analysis for Europe as a whole was provided by EUROCARE-4 for patients aged 15–24 years who were diagnosed in 1995–2002.

Added value of this study

The present EUROCARE-5 study provides the latest population-based, 5-year relative survival estimates for European AYAs (aged 15–39 years at diagnosis) compared with children (0–14 years) and adults (40–69 years), diagnosed with cancer in 2000–07. The study also provides survival time trends (1999–2007) for AYAs and children, and assesses whether survival improvements in AYAs still lag behind those in children; and, for the first time to our knowledge, analyses survival differences between AYAs and adults. We found that survival improved during the study period for both AYAs and children with cancer in Europe, and that survival improvements were similar in both these age categories. This finding contrasts with previous results that AYAs lag behind children in terms of survival improvement. However, survival remained significantly worse in AYAs than in children for acute lymphoid leukaemia, acute myeloid leukaemia, Hodgkin's lymphoma, non-Hodgkin lymphoma, astrocytoma, Ewing's sarcoma of bone, rhabdomyosarcoma, and osteosarcoma; and for acute myeloid leukaemia, soft-tissue sarcomas, and fibrosarcomas, survival remained unchanged for AYAs over the study period. These findings are in line with data from earlier time periods (1995–2002).

Implications of all the available evidence

AYAs have worse survival than children for many cancers affecting both groups, justifying initiatives to improve outcomes for adolescents and young adults. For cancers affecting AYAs and children, it has been suggested that AYAs should be treated in an integrated paediatric–adult multidisciplinary setting. This integration would increase the likelihood of inclusion in clinical trails, and improve family and social support. For AYAs with acute lymphoid leukaemia, data clearly indicate that although tumour biology is relatively unfavourable in this group, application of paediatric treatment protocols is feasibile and improves outcomes. However, robust evidence that regimens used to treat children actually benefit AYAs is only available for acute lymphoid leukaemia. Thus, further studies are needed to understand why survival improvements in AYAs lag behind those in children for many important cancers affecting both. The time of these analyses (patients diagnosed in 2000–07, and followed up until at least the end of 2008) pre-dates implementation of European initiatives to improve outcomes, and thus provides important baseline data to evaluate whether initiatives will lead to improved survival in European AYAs with cancer.

Methods

Study design and data collection

We used data provided by European population-based cancer registries participating in EUROCARE-5.[11] Registries provided information on the site and morphology of each cancer diagnosed, which was coded according to the International Classification of Disease for Oncology third revision (ICD-O-3).[12] Data for AYAs and for adults were provided by 97 of the 99 cancer registries contributing to the EUROCARE-5 adult database.[13]

Data for cancers in children were supplied by 72 of the 74 cancer registries contributing to the EUROCARE-5 childhood database.[14] These registries were the same as those that provided data for AYA and adult cancers for 21 of 27 countries (Finland, Iceland, Norway, Sweden, Ireland, Northern Ireland, Scotland, Austria, Belgium, Netherlands, Switzerland, Croatia, Malta, Portugal, Slovenia, Bulgaria, Estonia, Latvia, Lithuania, Poland, and Slovakia). For the remaining six

countries (England, France, Germany, Italy, Spain, and Wales), data from specialised childhood registries were used instead, which were generally national (in one case supranational, the England and Wales childhood cancer registry) rather than the several subnational registries used for adult cancers, maximising population coverage. Preliminary analysis showed that childhood survival results were the same irrespective of whether data from specialised or general registries were used. Table 1 shows the population coverage of cancer registration (children and adults) in each of the 27 countries in this study.

Table 1. Cancer cases in adolescents (aged 15–19 years) and young adults (20–39 years) diagnosed in 2000–07, in 27 European countries, with data quality indicators

	2000–07							2000–03 lost to follow-up[*]	Percentage of population covered by cancer registration (%)		Included in time trend analysis
	Age 15–19 years	Age 20–39 years	Death certificate only or by autopsy cases[†]	Major errors	Patients included in analysis	Microscopically verified	Unspecified cases[‡]		Adult database	Childhood database	
Finland	565 (8·3%)	6276 (91·7%)	28 (0·4%)	5 (0·1%)	6808	6756 (99·2%)	160 (2·4%)	17 (0·5%)	100%	100%	Yes
Iceland	59 (9·8%)	540 (90·2%)	2 (0·3%)	0	596	592 (99·3%)	7 (1·2%)	0	100%	100%	Yes
Norway	446 (5·6%)	7574 (94·4%)	17 (0·2%)	72 (0·9%)	7930	7850 (99·0%)	115 (1·5%)	29 (0·8%)	100%	100%	Yes
Sweden	661 (5·6%)	11 228 (94·4%)	20 (0·2%)	18 (0·2%)	11 848	11 806 (99·6%)	295 (2·5%)	50 (0·9%)	100%	100%	Yes
England	4522 (5·6%)	75 787 (94·4%)	378 (0·5%)	522 (0·6%)	79 409	76 007 (95·7%)	2445 (3·1%)	240 (0·6%)	100%	100%[§]	Yes
Ireland	507 (7·3%)	6392 (92·7%)	16 (0·2%)	47 (0·7%)	6836	6709 (98·1%)	217 (3·2%)	0	100%	100%	Yes
Northern Ireland	466 (5·6%)	7861 (94·4%)	16 (0·2%)	16 (0·2%)	8294	8200 (98·9%)	141 (1·7%)	6 (0·1%)	100%	100%	Yes
Scotland	287 (6·6%)	4064 (93·4%)	14 (0·3%)	2 (0·05%)	4335	3723 (85·9%)	222 (5·1%)	0	100%	100%	Yes
Wales	169 (6·0%)	2638 (94·0%)	7 (0·2%)	61 (2·2%)	2739	2622 (95·7%)	162 (5·9%)	0	100%	100%[§]	Yes
Austria	786 (6·0%)	12 250 (94·0%)	166 (1·3%)	60 (0·5%)	12 810	12 698 (99·1%)	342 (2·7%)	0	100%	100%	Yes
Belgium	652 (6·2%)	9942 (93·8%)	0	0	10 189	9961 (97·8%)	276 (2·7%)	0	58%	56%	No
France	606 (6·9%)	8230 (93·1%)	0	12 (0·1%)	8590	8520 (99·2%)	118 (1·4%)	137 (2·2%)	23%	100%[§]	No

	2000–07							2000–03 lost to follow-up[*]	Percentage of population covered by cancer registration (%)		Included in time trend analysis
	Age 15–19 years	Age 20–39 years	Death certificate only or by autopsy cases[†]	Major errors	Patients included in analysis	Microscopically verified	Unspecified cases[‡]		Adult database	Childhood database	
Germany	1610 (5·8%)	25 959 (94·2%)	417 (1·5%)	30 (0·1%)	27 034	26 497 (98·0%)	620 (2·3%)	402 (3·0%)	23%	100%[§]	Yes[¶]
Netherlands	1577 (5·4%)	27 524 (94·6%)	17 (0·1%)	0	29 083	28 894 (99·4%)	279 (1·0%)	241 (1·7%)	100%	100%	Yes
Switzerland	247 (6·2%)	3714 (93·8%)	8 (0·2%)	7 (0·2%)	3881	3867 (99·6%)	33 (0·9%)	185 (9·7%)	30%	29%	Yes[¶]
Croatia	490 (6·6%)	6921 (93·4%)	40 (0·5%)	6 (0·1%)	7365	6202 (84·2%)	1351 (18·3%)	0	100%	100%	No
Italy	1514 (4·8%)	30 050 (95·2%)	49 (0·2%)	84 (0·3%)	31 389	29 719 (94·7%)	2158 (6·9%)	409 (2·3%)	35%	36%[§]	Yes[¶]
Malta	52 (9·6%)	488 (90·4%)	2 (0·4%)	5 (0·9%)	524	505 (96·4%)	14 (2·7%)	0	100%	100%	Yes
Portugal	585 (5·5%)	10 125 (94·5%)	0	66 (0·6%)	10 461	10 257 (98·0%)	373 (3·6%)	70 (1·1%)	76%	70%	No
Slovenia	196 (5·6%)	3311 (94·4%)	6 (0·2%)	0	3501	3487 (99·6%)	40 (1·1%)	0	100%	100%	Yes
Spain	393 (5·3%)	7007 (94·7%)	42 (0·6%)	2 (0·03%)	7234	7111 (98·3%)	203 (2·8%)	59 (1·1%)	17%	34%[§]	Yes[¶]
Bulgaria	576 (5·3%)	10 291 (94·7%)	335 (3·1%)	7 (0·1%)	10 525	10 081 (95·8%)	641 (6·1%)	25 (0·5%)	100%	100%	Yes
Estonia	140 (8·1%)	1591 (91·9%)	10 (0·6%)	3 (0·2%)	1716	1678 (97·8%)	62 (3·6%)	5 (0·6%)	100%	100%	Yes
Latvia	229 (8·5%)	2475 (91·5%)	100 (3·7%)	39 (1·4%)	2565	2408 (93·9%)	276 (10·8%)	0	100%	100%	No
Lithuania	294 (6·9%)	3967 (93·1%)	43 (1·0%)	10 (0·2%)	4193	4030 (96·1%)	367 (8·8%)	39 (1·7%)	100%	100%	Yes
Poland	540 (9·1%)	5374 (90·9%)	25 (0·4%)	86 (1·5%)	5760	4883 (84·8%)	889 (15·4%)	77 (2·7%)	13%	12%	Yes[¶]
Slovakia	552 (7·8%)	6499 (92·2%)	181 (2·6%)	2 (0·03%)	6868	6549 (95·4%)	202 (2·9%)	0	100%	100%	Yes

Data are n (%) and n, unless otherwise stated. Also shown are the percentages of the country populations covered by the adult and childhood databases, and the countries included in the survival time-trend analyses. Major errors include missing or invalid data items.

* Proportion of patients diagnosed in 2000–03 and lost to follow-up (alive with less than 5 years of follow-up); for the French registries this quality indicator was calculated for cases diagnosed in 2000–02.

† Data for death certificate only cases unavailable for Sweden, Belgium, France, Netherlands, and Portugal because death certificate information is not used to initiate cancer registration.

‡ Consisting the following International Classification of Childhood Cancers third edition diagnostic groups: Ie, IIe, IIIf, VIc, VIIc, VIIIe, IXe, Xe, and XIIb.

§ Specialised childhood cancer registry.

¶ Registries in countries without 100% population coverage but uninterrupted data from 1995 to 2007, and included in the time-trend analyses are: in Germany (Hamburg and Saarland), in Switzerland (Basel, Geneva, Grisons, St Gallen, and Valais), in Italy (Biella, Ferrara, Friuli Venezia Giulia, Liguria Mesothelioma, Latina, Modena, Napoli, Parma, Ragusa, Reggio Emilia, Romagna, Sassari, Torino, Trentino, Umbria), in Spain (Girona), and in Poland (Cracow, Kielce, and Silesia).

All primary malignant cancers were included in the analyses, except non-melanoma skin cancers and pilocytic astrocytoma. Pilocytic astrocytoma is the most common CNS neoplasm in children but it was excluded because it has a borderline ICD-O-3 behaviour code. Non-melanoma skin cancers were excluded because cancer registry data on these cancers is generally incomplete. If two or more cancers were diagnosed in a patient, all were included thus we estimated survival for a particular cancer diagnosis and not a particular individual. Cancers were grouped into 46 diagnostic categories: 19 non-carcinoma categories (affecting AYAs and children) and 27 carcinoma categories (affecting AYAs and adults), as defined by the International Classification of Childhood Cancers third edition (ICCC-3;[15]appendix p 1).

Statistical analysis

We estimated 5-year relative survival for cancers diagnosed in children, AYAs, and adults, in 27 European countries in 2000–07, who were followed up until at least Dec 31, 2008. Relative survival is the ratio of observed survival in patients with cancer to expected survival for individuals in the general population matched by age, sex, and time period. We estimated expected survival by the Ederer II method.[16] Relative survival is an estimate of cancer-specific survival because it removes the effect of mortality due to competing causes, which can vary widely between countries. We used the so-called complete method to estimate 5-year relative survival.[17] This method is similar to the established cohort method,[16] but also includes the most recently diagnosed patients (in this study, those diagnosed in 2004–07) who do not have 5 years of follow-up.

To provide valid estimates of European survival we applied population weightings to region-specific relative survival estimates to correct for differing numbers of children, AYAs, and adults in the five different regions of Europe (northern [Finland, Iceland, Norway, and Sweden], central [Austria, Belgium, France, Germany, Netherlands, and Switzerland], southern [Croatia, Italy,

Malta, Portugal, Slovenia, and Spain], and eastern Europe [Bulgaria, Estonia, Latvia, Lithuania, Poland, and Slovakia], and the UK and Ireland [England, Ireland, Northern Ireland, Scotland, and Wales]). For cancers in patients aged 0–39 years at diagnosis, the weightings applied to relative survival estimates for each European region consisted of the ratio of the population of that age in the region in 2000–07, to that of the European population of the same age in the same period. For adults aged 40–69 years with cancer, the weightings were derived from the entire adult population (those aged 15–99 years) of each European region and Europe as a whole.[13]

We compared 5-year relative survival between children (0–14 years) and adolescents (15–19 years); between children and young adults (20–39 years); between children and AYAs; and between AYAs and adults. The significance of survival differences was assessed by the *Z* test, assuming as null hypothesis that differences between each pair of relative survival estimates were normally distributed with zero mean, and that the variance was given by the sum of the corresponding variances. P values less than 0·05 were considered to be significant.

To assess changes in 5-year relative survival from 1999 to 2007 we used only cancer registries providing uninterrupted data from at least 1995 to 2007. 43 registries were identified with uninterrupted data for AYAs (table 1), and 41 of 43 registries previously identified by Gatta and colleagues[14] were used that had uninterrupted data for children (except the registries of Hungary and Denmark). To provide reliable predictions for recently diagnosed patients, we estimated 5-year relative survival using the period approach.17, 18 We defined three periods: patients in follow-up in 1999–2001 (diagnosed during 1995–2001); patients in follow-up in 2002–04 (diagnosed during 1998–2004); and patients in follow-up in 2005–07 (diagnosed during 2001–07). For these three periods, the last year of follow-up and last year of diagnosis do not coincide exactly; for example, the period estimate for 2005–07 includes follow-up information in 2008 and incidence data up to 2007.[19]

For cancers that did not seem to have a linear change in relative survival with time we tested linearity, by comparing a model assuming linear change with time with a model in which time changed quadratically. We then used the likelihood ratio test to compare the two models and hence exclude a non-linear change in relative survival over time (appendix p 3).

We present time trends in 5-year relative survival for children, adolescents, young adults, and AYAs, for all cancers combined and for the major diagnostic groups whose survival changed significantly during the study period. For all cancers combined, survival was casemix-adjusted by multiplying the relative survival of each diagnostic category with weightings proportional to the corresponding numbers of cases in children, adolescents, young adults, and AYAs, and adding together these figures. Diagnostic categories that contributed to combined survival of all cancers were acute lymphoid leukaemias, acute myeloid leukaemia, Hodgkin's lymphoma, non-Hodgkin lymphoma, CNS and miscellaneous intracranial and intraspinal neoplasms, osteosarcomas, chondrosarcomas, Ewing's sarcoma, soft-tissue sarcomas, germ-cell tumours, melanoma, and carcinomas of thyroid, breast, colorectum, appendix, male genital tract, female genital tract, urinary tract, head and neck, liver, lung and trachea (appendix p 1), and other cancers as a single group (all cancers in the databases that do not fit into the 19 diagnostic categories of cancers affecting both children and AYAs, or the 27 carcinomas affecting both AYAs and adults).

To obtain mean yearly changes in mortality for 1999–2007, for Europe as a whole, we modelled relative survival using a generalised linear model. We assumed that the number of reported deaths in each time interval, calculated as the sum of the excepted deaths in the general population and the excess deaths due to cancer, followed a Poisson distribution. The model included sex, 5-year age groups, and country as categorical variables and time of follow-up and year of diagnosis as

continuous variables. Diagnostic category was only included as covariate in the model for all cancers combined. A separate model was fitted to each diagnostic category and to each age group (ie, children, adolescents, young adults, and AYAs). The probability of the relative excess risk of death not being one was assessed by the two-tailed Wald test.

We next compared the relative excess risks of death estimated in children with those estimated in patients aged 15–19 years, 20–39 years, and 15–39 years. We assessed the significance of these differences using the *Z* test, assuming that differences in the logarithm of the relative excess risk of death had a normal distribution. We did the analyses with SEER*Stat (version 8.1.5), Microsoft Excel (version 2007), and Stata (version 13).

Results

Table 1 shows the numbers of cancers in AYAs, diagnosed in 2000–07, with main data quality indicators for both combined (adolescents and young adults) by country. 18 721 (6%) of 316 799 cancers occurred in adolescents and 298 078 (94%) of 316 799 cancers occurred in young adults. Only 4316 (1·4%) of 316 799 cancers in AYAs were excluded: 1939 (0·6%) cancers because these were ascertained from death certificate or autopsy only; 1215 (0·4%) because these were censored immediately after diagnosis (had no follow-up); and 1162 (0·4%) because the records contained non-recoverable major errors (missing or invalid data items).

Most cancers were microscopically verified (table 1). Scotland, Poland, and Croatia had the lowest proportions of microscopically verified cancers; for all other countries microscopic verification was 93·9–99·6% (table 1). For 12 008 (3·8%) of 312 483 cancers, ICCC-3 morphology was unspecified. Croatia, Poland, and Latvia had the highest proportions of cancers with unspecified morphology; most (15) other countries had less than 3% unspecified morphology (table 1). Only 1991 (1·2%) of 160 981 cancers diagnosed in 2000–03 were lost during follow-up. Switzerland had the greatest percentage of cancer cases loss to follow-up (9·7%), followed by Germany (3·0%), Poland (2·7%), Italy (2·3%), and France (2·2%; table 1).

We estimated 5-year relative survival for 56 505 cancers diagnosed in children, 312 483 cancers in AYAs, and 3 567 383 cancers in adults. 5-year relative survival for all cancers combined was 76% (95% CI 75·3–76·8) for children, and 79% (78·9–79·3) for AYAs (appendix p 3), with no sex difference for children, but better survival for female compared with male AYAs (figure 1). Cancers with a good prognosis (Hodgkin's lymphoma, non-Hodgkin lymphoma, germ-cell tumours, melanoma, thyroid carcinoma, and breast carcinoma), were more frequent in AYAs (179 322 [57%] of 312 483 cancers) than in children (8305 [15%] of 56 505 cancers). Female AYAs had a slightly higher proportion of cancers with a good prognosis (eg, skin melanoma and thyroid cancer) than male AYAs (appendix p 4). Survival was better for female than male AYAs for acute myeloid leukaemias, Hodgkin's lymphoma, non-Hodgkin lymphoma, CNS neoplasms, soft-tissue sarcomas, melanoma, and thyroid carcinoma, breast carcinoma, head and neck carcinoma, lung carcinoma, and tracheal carcinoma (appendix p 4). 5-year relative survival was slightly better for male than for female AYAs with urinary tract carcinomas and gonadal germ-cell tumours. For the remaining cancer types (with at least 200 male cases and 200 female cases), no significant differences were found in 5-year relative survival between male and female AYAs (appendix p 4).

Table 2 shows 5-year relative survival by 5-year age categories for the 19 non-carcinomas and 27 carcinomas affecting AYAs. Haemopoietic malignancies were the most common cancers in the 15–24 year age class, as in children. For all ages of AYAs, 5-year relative survival was greater than 90% for Hodgkin's lymphoma, about 77% for non-Hodgkin lymphoma, and was relatively low for acute lymphoid leukaemias (46% to 62%) and acute myeloid leukaemias (about 50%). Gonadal

germ-cell tumours and skin melanoma were the second and third most common cancers in AYAs; both had 5-year relative survival of 88% or higher in all age groups.

Table 2. 5-year relative survival estimates for major cancers affecting European adolescents[*] and young adults[†] diagnosed in 2000–07

	15–19 years[*]		20–24 years[†]		25–29 years[†]		30–34 years[†]		35–39 years[†]	
	N	Relative survival (SE)	N	Relative survival (SE)	N	Relative survival (SE)	N	Relative survival (SE)	N	Relative survival (SE)
Acute lymphoid leukaemia	1378	62·2% (1·6)	797	45·6% (2·0)	585	47·8% (2·4)	762	53·6% (2·1)	1095	60·5% (1·8)
Acute myeloid leukaemia	704	52·2% (2·2)	819	55·2% (2·1)	1018	47·7% (1·8)	1104	49·3% (1·7)	1544	47·3% (1·5)
Hodgkin's lymphomas	3541	94·3% (0·5)	4457	93·9% (0·4)	4164	93·9% (0·5)	3816	91·6% (0·6)	3300	90·2% (0·7)
Non-Hodgkin lymphoma (excluding Burkitt's lymphoma)	1217	78·0% (1·4)	1667	76·3% (1·2)	2361	77·8% (1·0)	3762	78·0% (0·8)	6052	76·9% (0·7)
CNS and miscellaneous intracranial and intraspinal neoplasms	1464	61·8% (1·5)	1804	63·4% (1·4)	2652	60·1% (1·1)	3774	57·4% (1·0)	4509	49·8% (0·9)
Astrocytomas	604	50·8% (2·5)	850	54·2% (2·2)	1392	51·5% (1·7)	2056	47·6% (1·4)	2515	38·7% (1·2)
Intracranial and intraspinal embryonal neoplasms	233	67·0% (3·8)	187	61·3% (4·3)	156	60·0% (4·2)	145	53·3% (4·9)	105	56·1% (6·0)
Medulloblastomas	158	72·8% (4·5)	127	63·3% (4·8)	112	69·0% (5·3)	85	65·7% (5·7)	64	66·2% (7·0)
Osteosarcomas	765	60·3% (2·2)	353	61·4% (3·2)	185	65·3% (4·0)	163	65·2% (4·7)	162	60·1% (4·4)
Chondrosarcomas	140	80·7% (3·8)	134	80·5% (3·8)	162	85·5% (3·0)	245	82·7% (3·0)	313	83·1% (2·5)
Ewing's sarcoma and related sarcomas of bone	448	51·1% (2·7)	241	50·4% (3·7)	136	45·3% (5·9)	112	47·7% (5·5)	75	42·9% (6·5)
Soft-tissue and other extraosseous sarcomas (excluding Kaposi)	1185	63·0% (1·6)	1365	66·3% (1·5)	1699	68·5% (1·4)	2186	73·3% (1·1)	3062	72·2% (0·9)
Rhabdomyosarcomas	280	39·6% (3·4)	155	35·8% (4·7)	84	30·9% (6·0)	74	39·0% (7·1)	83	43·2% (5·9)
Fibrosarcomas	47	72·8% (9·8)	85	88·6% (3·6)	117	78·9% (5·0)	156	88·4% (3·0)	223	74·7% (3·7)
Germ-cell tumours, trophoblastic tumours, and neoplasms of gonads	2238	92·2% (0·7)	5892	93·5% (0·4)	8991	95·2% (0·3)	9559	95·6% (0·3)	8885	94·7% (0·3)
Intracranial and intraspinal germ-cell tumours	158	79·5% (4·2)	79	86·3% (5·1)	41	83·8% (6·2)	28	81·2% (6·2)	4	100% (0)
Malignant gonadal germ-cell tumours	2011	93·6% (0·7)	5632	94·3% (0·4)	8715	95·9% (0·3)	9318	96·1% (0·3)	8684	95·4% (0·3)
Malignant melanomas	1292	90·8% (1·2)	3772	90·9% (0·7)	6677	90·5% (0·5)	10 500	89·4% (0·5)	14 113	87·1% (0·4)
Skin melanoma	1248	91·2% (1·2)	3669	91·2% (0·7)	6478	91·3% (0·5)	10 150	90·2% (0·5)	13 582	88·1% (0·4)
Thyroid carcinomas	1063	99·7% (0·2)	2205	99·0% (0·3)	3778	99·3% (0·2)	5432	99·1% (0·2)	6918	98·9% (0·2)
Breast carcinomas	53	87·3% (5·6)	550	82·9% (2·1)	3801	78·1% (0·9)	13 813	81·4% (0·4)	34 370	84·9% (0·3)
Colorectal carcinomas (excluding carcinoids)	98	54·0% (6·5)	567	57·7% (2·5)	1220	57·0% (1·6)	2948	61·4% (0·9)	6524	62·4% (0·6)
Appendix carcinoma (excluding carcinoids)	27	100·0% (0)	44	78·8% (2·6)	59	84·3% (4·6)	115	77·8% (5·2)	147	71·1% (5·1)
Male genital tract carcinomas	21	83·8% (8·9)	85	88·0% (3·8)	126	80·8% (4·2)	161	76·7% (4·3)	418	77·9% (2·7)
Testicular	16	82·6% (9·1)	76	89·2% (3·9)	77	87·9% (4·0)	64	85·5% (5·3)	58	87% (4·3)
Penile	1	100·0% (0)	4	75·0% (21·7)	26	77·2% (9·3)	74	56·7% (6·3)	213	76·5% (4·0)
Prostate	3	66·7% (27·2)	5	80·1% (17·9)	18	67·1% (16·6)	20	76·2% (10·4)	137	81·2% (5·1)
Female genital tract carcinomas	197	80·5% (3·9)	1324	84·7% (1·4)	4781	83·3% (0·7)	9940	83·0% (0·5)	15 230	80·1% (0·4)
Ovarian	154	81·1% (4·2)	423	81·8% (2·3)	836	76·5% (1·8)	1483	72·7% (1·4)	2869	69·9% (1·0)
Uterine cervix	37	76·0% (10·0)	846	87·1% (1·6)	3735	84·8% (0·8)	7802	84·9% (0·5)	10 632	81·6% (0·4)
Corpus uteri and uterine not otherwise specified	0	..	28	81·0% (6·2)	117	89·3% (4·8)	428	91·9% (1·6)	1253	89·5% (1·1)
Corpus uteri	0	..	25	86·5% (6·0)	113	89·4% (4·8)	413	92·0% (1·6)	1218	89·2% (1·1)
Urinary tract carcinomas	142	83·8% (3·4)	317	82·0% (2·5)	749	84·4% (1·6)	1752	84·6% (1·0)	3990	81·8% (0·7)
Kidney	93	77·6% (4·8)	181	78·1% (3·2)	467	82·7% (2·1)	1099	85·8% (1·2)	2603	82·3% (0·8)
Bladder	47	98·7% (1·3)	134	85·1% (4·9)	270	84·4% (3·1)	616	81·0% (1·9)	1284	79·9% (1·3)
Head and neck carcinomas	340	84·4% (2·3)	488	81·1% (2·1)	804	81·3% (1·6)	1610	73·9% (1·4)	3691	63·8% (0·9)
Nasal cavity and sinuses	8	NE	20	59·9% (8·7)	41	56·5% (9·2)	119	62·6% (5·1)	196	59·0% (4·2)
Nasopharynx	129	74·5% (5·3)	127	76·3% (4·5)	124	71·3% (4·7)	199	66·5% (3·9)	368	68·1% (2·7)
Salivary gland	119	94·0% (2·9)	153	93·5% (2·3)	240	92·3% (2·2)	323	87·0% (2·5)	468	83·0% (2·2)
Hypopharynx	1	100·0% (0)	1	NE	8	29·3% (0)	26	46·5% (10·7)	159	31·3% (3·9)
Larynx	10	100·0% (0)	16	93·4% (6·4)	44	89·5% (5·5)	131	72·6% (4·6)	530	71·3% (2·2)

	15–19 years*		20–24 years†		25–29 years†		30–34 years†		35–39 years†	
	N	Relative survival (SE)	N	Relative survival (SE)	N	Relative survival (SE)	N	Relative survival (SE)	N	Relative survival (SE)
Oropharynx carcinoma	15	93·4% (6·4)	32	74·2% (7·7)	74	78·5% (6·7)	180	70·0% (4·2)	684	50·5% (2·1)
Oral cavity carcinoma	48	87·0% (4·0)	120	74·0% (4·5)	239	77·6% (3·4)	537	71·3% (2·4)	1097	61·6% (1·8)
Lip carcinoma	6	66·7% (19·2)	12	74·4% (18·3)	27	98·9% (1·0)	71	95·4% (2·0)	153	93·7% (2·1)
Liver and intrahepatic bile duct carcinomas	95	16·0% (5·2)	119	31·4% (5·6)	175	35·5% (4·4)	344	21·1% (2·6)	564	26·1% (2·3)
Lung and trachea carcinomas	103	87·1% (4·1)	208	71·4% (3·5)	462	54·2% (2·7)	1112	38·9% (1·6)	3552	23·5% (0·8)

Survival figures are population weighted. NE=not estimable. SE=standard error of the relative survival ratio.

* Adolescents (aged 15–19 years).

† Young adults (aged 20–39 years).

For CNS neoplasms, 5-year relative survival was about 60% in patients aged up to 29 years, and was lower in older age classes, especially for astrocytomas (to around 41%). Osteosarcoma and Ewing's sarcoma were the most common bone sarcomas in adolescents (aged 15–19 years) and those aged 20–24 years, whereas chondrosarcomas, as a proportion of all bone sarcomas, increased progressively in those from ages 20–24 years and older. 5-year relative survival was good for osteosarcoma and chondrosarcoma. For Ewing's sarcoma 5-year relative survival reduction across age categories was not significant (p=0·24), whereas for soft-tissue sarcomas, 5-year relative survival significantly increased across age catgeories (p<0·0001).

Carcinomas were rarely diagnosed in AYAs, but occurrence increased with advancing age from 25–29 years and older (table 2). In adolescents, thyroid carcinoma was the most common carcinoma and had excellent 5-year relative survival (99·7%). Head and neck carcinomas (mainly at nasopharyngeal and salivary gland sites) were the second most common carcinomas in adolescents, followed by colorectal and ovarian carcinomas (all with good or fairly good survival). For most other carcinomas in adolescents, 5-year relative survival was greater than 75% (except for liver carcinoma at <20%).

In young adults, female genital tract and breast carcinomas were the most common malignancies, with 5-year relative survival about 80% in all age classes (table 2); cervical carcinoma was the most common female genital tract carcinoma, with high 5-year relative survival in all age groups. Other relatively common carcinomas in young adults were thyroid and colorectal carcinomas, with excellent (99%) 5-year relative survival for thyroid, and intermediate (about 60%) relative survival for colorectal carcinomas (excluding carcinoids). 5-year relative survival for male genital and head and neck carcinomas declined with with advancing age as the site of occurrence changed (table 2). 5-year relative survival declined substantially with age for carcinomas of the lung and trachea (table 2), in relation to an age-related decline in the proportion of well differentiated carcinoids (73% in adolescents; 13% in those aged 35–39 years). 5-year relative survival for liver carcinomas was poor for all AYA age categories.

Table 3 compares 5-year relative survival in children with that in adolescents, young adults, and AYAs, for the 19 diagnostic cancers categories affecting children and AYAs (appendix p 1). AYAs had significantly worse survival than children for acute lymphoid leukaemias, acute myeloid leukaemias, Hodgkin's lymphoma, non-Hodgkin lymphoma, astrocytomas, Ewing's sarcoma of

bone, rhabdomyosarcoma, and osteosarcoma (table 3). AYAs had significantly better survival than children for medulloblastomas and germ-cell tumours. Survival differences between children and adolescents, and children and young adults, were similar to the differences between children and AYAs for most cancers in table 3.

Table 3. 5-year relative survival in European children in comparison to survival in adolescents, young adults, and AYAs for major cancers affecting children and AYAs diagnosed in 2000–07

	Children (0–14 years)		Adolescents (15–19 years)			Young adults (20–39 years)			AYAs (15–39 years)		
	N	Relative survival (SE)	N	Relative survival (SE)	p value*	N	Relative survival (SE)	p value*	N	Relative survival (SE)	p value*
Acute lymphoid leukaemias	15 089	85·8% (0·4)	1378	62·2% (1·6)	<0·0001	3239	52·8% (0·01)	<0·0001	4617	55·6% (0·9)	<0·0001
Acute myeloid leukaemias	2944	60·5% (1·0)	704	52·2% (2·2)	0·0007	4484	49·4% (0·9)	<0·0001	5188	49·8% (0·8)	<0·0001
Hodgkin's lymphomas	2995	95·1% (0·5)	3541	94·3% (0·5)	0·21	15 735	92·6% (0·3)	<0·0001	19 276	92·9% (0·2)	<0·0001
Non-Hodgkin lymphomas (excluding Burkitt's lymphoma)	2407	83·0% (0·9)	1217	78·0% (1·4)	0·0023	13 840	77·3% (0·4)	<0·0001	15 057	77·4% (0·4)	<0·0001
CNS and miscellaneous intracranial or intraspinal neoplasms	8856	57·2% (0·6)	1464	61·8% (1·5)	0·0090	12 722	56·1% (0·5)	0·15	14 184	56·8% (0·5)	0·52
Astrocytomas	2584	61·9% (1·1)	604	50·8% (2·5)	0·0003	6803	46·0% (0·7)	<0·0001	7405	46·4% (0·7)	<0·0001
Intracranial and intraspinal embryonal neoplasms	2951	56·3% (1·1)	233	67·0% (3·8)	0·0074	593	57·8% (2·4)	0·51	826	60·3% (2·0)	0·074
Medulloblastomas	2156	63·2% (1·3)	158	72·8% (4·5)	0·041	388	67·4% (2·8)	0·15	546	69·3% (2·3)	0·020
Osteosarcoma	1430	66·8% (1·5)	765	60·3% (2·2)	0·012	863	62·5% (1·9)	0·070	1627	61·5% (1·5)	0·011
Chondrosarcoma	66	89·4% (3·4)	140	80·7% (3·8)	0·092	854	83·0% (1·5)	0·084	994	82·6% (1·4)	0·064
Ewing's sarcoma and related sarcomas of bone	1322	66·6% (1·5)	448	51·1% (2·7)	<0·0001	564	47·4% (2·5)	<0·0001	1012	49·3% (1·8)	<0·0001
Soft-tissue and other extraosseous sarcomas (excluding Kaposi)	3871	69·3% (0·9)	1185	63·0% (1·6)	0·0007	8310	70·8% (0·6)	0·19	9493	69·8% (0·5)	0·66
Rhabdomyosarcomas	2124	66·6% (1·3)	280	39·6% (3·4)	<0·0001	396	36·4% (2·8)	<0·0001	675	37·8% (2·2)	<0·0001
Fibrosarcomas	209	83·8% (3·6)	47	72·8% (9·8)	0·29	581	81·5% (2·0)	0·60	628	81·4% (1·9)	0·56
Germ-cell tumours, trophoblastic tumours, and neoplasms of gonads	1805	91·5% (0·8)	2238	92·2% (0·7)	0·55	33 272	94·9% (0·2)	<0·0001	35 503	94·7% (0·1)	0·00013
Intracranial and intraspinal germ-cell tumours	466	85·9% (2·2)	158	79·5% (4·2)	0·18	152	79·0 %(4·2)	0·13	310	79·5% (2·9)	0·077
Malignant gonadal germ-cell tumours	821	96·8% (0·8)	2011	93·6% (0·7)	0·0015	32 295	95·6% (0·2)	0·11	34 300	95·4% (0·1)	0·078
Malignant melanomas	435	90·1% (1·7)	1292	90·8% (1·2)	0·70	34 994	88·9% (0·3)	0·47	36 279	88·9% (0·3)	0·50
Skin melanoma	394	92·2% (1·6)	1248	91·2% (1·2)	0·64	33 814	89·7% (0·3)	0·14	35 055	89·7% (0·3)	0·15

Relative survival data are population weighted. AYAs=adolescents and young adults. SE=standard error of the relative survival ratio.

*

For comparison with children (aged 0–14 years).

Table 4 compares 5-year relative survival in AYAs with that in adults for the 27 carcinomas affecting both age groups. For most carcinomas, survival was better for AYAs than for adults, with some notable exceptions such as colorectal, breast, and prostate carcinomas. 5-year survival for colorectal cancer was similar for AYAs and adults; for both breast and prostate carcinoma survival was significantly lower for AYAs than adults (table 4).

Table 4. 5-year relative survival in European AYAs in comparison with survival in adults for major carcinomas affecting AYAs and adults for cases diagnosed in 2000–07

	AYAs (15–39 years)		Adults (40–69 years)		p value (15–39 years *vs* 40–69 years)
	N	Relative survival (SE)	N	Relative survival (SE)	
Malignant melanomas	36 279	88·9% (0·3)	104 019	82·4% (0·2)	<0·0001
Thyroid carcinomas	19 396	99·2% (0·1)	45 834	93·1% (0·2)	<0·0001
Breast carcinomas	52 468	83·5% (0·2)	658 113	87·0% (0·1)	<0·0001
Colorectal carcinomas (excluding carcinoids)	11 344	61·3% (0·5)	395 525	60·8% (0·1)	0·49
Appendix carcinoma (excluding carcinoids)	392	77·2% (3·7)	2273	61·0% (1·5)	0·0001
Male genital tract carcinomas	811	80·1% (1·8)	406 036	89·6% (0·1)	<0·0001
Testicular	291	87·5% (2·3)	220	72·3% (3·6)	0·00034
Penile	318	72·8% (3·8)	5327	70·5% (0·9)	0·55
Prostate	183	79·9% (4·0)	400 311	89·8% (0·1)	0·014
Female genital tract carcinomas	31 460	81·6% (0·3)	237 360	69·1% (0·1)	<0·0001
Ovarian	5763	72·8% (0·7)	75 605	47·1% (0·2)	<0·0001
Cervix uteri	23 050	83·3% (0·3)	50 536	67·7% (0·3)	<0·0001
Corpus uteri and uterus not otherwise specified	1826	90·0% (0·9)	101 293	86·7% (0·2)	0·00025
Corpus uteri	1769	89·9% (0·9)	100 017	87·0% (0·2)	0·00073
Urinary tract carcinomas	6942	82·9% (0·9)	206 536	69·5% (0·1)	<0·0001
Kidney	4437	83·0% (0·6)	92 194	70·7% (0·2)	<0·0001
Bladder	2351	81·4% (1·0)	106 194	69·1% (0·2)	<0·0001
Head and neck carcinomas	6929	69·9% (0·6)	166 146	51·5% (0·1)	<0·0001
Nasal cavity and sinuses	383	60·2% (3·0)	4854	53·0% (0·9)	0·021
Nasopharynx	947	69·9% (1·7)	4839	51·2% (0·9)	<0·0001
Salivary gland	1303	88·2% (1·1)	6861	64·4% (0·7)	<0·0001
Hypopharynx	195	34·3% (3·6)	15 631	26·2% (0·4)	0·024
Larynx	731	72·9% (1·8)	48 857	61·8% (0·3)	<0·0001
Oropharynx	985	57·5% (1·8)	39 354	42·0% (0·3)	<0·0001
Oral cavity	2041	66·7% (1·3)	37 749	48·3% (0·3)	<0·0001
Lip	268	92·2% (2·2)	6863	90·2% (0·6)	0·37
Liver and intrahepatic bile duct carcinomas	1297	25·2% (1·4)	36 887	14·2% (0·2)	<0·0001
Lung and trachea carcinomas	5437	32·1% (0·7)	379 762	14·9% (0·1)	<0·0001

Survival figures are population weighted. AYAs=adolescents and young adults. SE=standard error of the relative survival ratio.

5-year relative survival for all cancers combined increased significantly from 76% (95% CI 74·7–77·1) in 1999–2001, to 79% (77·2–79·4) in 2005–07 for children (p<0·0001); from 77% (77·2–79·4) to 80% (78·8–82·2) for adolescents (p<0·0001); and from 79% (78·2–80·7) to 83% (81·1–84·0) for young adults (p<0·0001), and from 79% (78·1–80·5) to 82% (81·1–83·3) for AYAs (p<0·0001; figure 2). 5-year relative survival improved significantly with time in all age groups for acute lymphoid leukaemias and non-Hodgkin lymphomas. 5-year relative survival improved significantly only in children for acute myeloid leukaemias, soft-tissue sarcoma, and fibrosarcoma. Survival improved significantly only in young adults for CNS tumours, astrocytomas, and melanoma (figure 2). For the all other diagnostic categories and all age classes, survival remained stable over the study period.

We found that relative excess risks of death differed between age groups for several cancers. For acute lymphoid leukaemias, relative excess risk of death reduced significantly more in adolescents than in children (p=0·015). For CNS tumours in general, relative excess risk of death reduced significantly more in young adults than in children (p=0·037); and for astrocytomas relative excess risk of death reduced significantly more in young adults than in children (p=0·0047). For

fibrosarcomas, relative excess risk of death reduced significantly more in children than in AYAs (p=0·015). For all other diagnostic categories with significant changes in survival over time, no significant differences in relative excess risk of death between children and AYAs were found (appendix p 5).

Discussion

Two major findings of our study were that survival improved over time (1999–2007) for both AYAs and children with cancer in Europe, and that the level of improvement was similar in both groups. Thus, the slower survival improvement reported by Bleyer and colleagues,[2] up to the 1990s for AYAs in the USA compared with children, seems not to be present in Europeans diagnosed more recently.

Another major finding of our study was that, overall, AYAs had slightly better 5-year relative survival than children (figure 1), mainly because cancers with good prognoses were more frequent in AYAs than in children. In fact survival in AYAs lagged behind that in children for several cancers that affect both groups, particularly for relatively common haemopoietic malignancies. Thus, 5-year relative survival was significantly worse in AYAs than in children for acute lymphoid leukaemias, acute myeloid leukaemias, Hodgkin's lymphoma, non-Hodgkin lymphoma, astrocytoma, Ewing's sarcoma of bone, rhabdomyosarcoma, and osteosarcoma (table 3). Furthermore, for acute myeloid leukaemias, soft-tissue sarcoma, and fibrosarcoma, survival remained unchanged for AYAs over the study period. These findings are consistent with data from earlier periods1, 2 and justify initiatives to improve cancer outcomes for AYAs in Europe.[8]

For cancers in AYAs that also affect children, it has been suggested that AYAs should be treated in an integrated paediatric–adult multidisciplinary setting.[8] This change should increase the likelihood of AYAs being included in clinical trials, and improve family and social support.[8] For acute lymphoid leukaemias, data clearly indicate that although tumour biology is relatively unfavourable in AYAs, application of treatment protocols for children is feasible and improves outcomes.20, 21, 22, 23

Of note, survival for acute lymphoid leukaemias in AYAs improved substantially over the study period (1999–2007), particularly in those aged 15–19 years (figure 2). By 2005–07, 5-year relative survival for acute lymphoid leukaemias had reached nearly 60%, compared with 50% for acute myeloid leukaemias. This is an important change since, in the previous EUROCARE period (1995–2002), survival of AYAs was worse for those with acute lymphoid leukaemias than acute myeloid leukaemias.[1] This improved survival for AYAs with acute lymphoid leukaemias probably reflects increasing use of paediatric treatment protocols in this older age group. Imatinib (plus chemotherapy) is indicated for adults and children with newly diagnosed Philadelphia chromosome-positive acute lymphoid leukaemia; thus increasing use of imatinib in AYAs with this form of leukaemia could have contributed to the improvement. However only a small percentage (3–11%) of AYAs with acute lymphoid leukaemias have this translocation.[24] Furthermore, treatment-related information was not systematically available from cancer registries and could not be analysed in this study. In general, whether chemotherapy regimens for children are appropriate for AYAs older than 20 years is unclear.[25]

In addition to advocating the development of integrated child and adult multidisciplinary models of care, greater inclusion in clinical trials, and research to improve treatments, the European Network for Teenagers and Young Adults with Cancer (created in the context of the ENCCA) is promoting the development of AYA-specific practice guidelines, education for cancer care, healthy lifestyles, and greater involvement of patients and patient support organisations.[8]

We also found that female AYAs had better survival than male AYAs (figure 1), mainly for acute myeloid leukaemias, Hodgkin's lymphoma, non-Hodgkin lymphoma, CNS neoplasms, soft-tissue sarcomas, and melanoma. Sex differences in adult cancer survival have been reported previously[26] with sex hormones proposed as the prime mediators of the survival advantage in women. Whether this explanation is applicable to AYAs is unclear and merits further study.

We found that AYAs had better survival for most cancers (carcinomas) that affect AYAs and adults, supporting the idea that young patients with few comorbidities are likely to do better than older patients. However, tumour biology (including gene expression alterations), histotype, and stage at diagnosis are also likely to influence survival in AYAs. Furthermore, casemix was more favourable in AYAs than adults for female genital tract cancers (cervix uteri: 23 050 [73%] of 31 460 cancers *vs* 50 536 [21%] of 237 360 cancers) and head and neck cancers (salivary gland cancer: 1303 [19%] of 6929 cancers *vs* 6861 [4%] of 166 146 cancers).

However, AYAs had worse survival than adults for breast and prostate carcinomas. For breast cancer, this might be because, compared with older women, young women present with larger, less hormone-sensitive, higher grade cancers, that have often spread to lymph nodes.27, 28 For prostate cancer, older men have biologically less aggressive disease than younger men. Additionally, because older men usually die sooner after diagnosis (due to causes unrelated to prostate cancer) compared with younger men, they are less likely to experience disease progression or develop treatment-related morbidities.29, 30

We do not present 1-year relative survival in this study; because of the good prognosis of most cancers we analysed, and the long life expectancy of the young population, 5-year relative survival was judged a good summary measure of cancer outcomes in AYAs. An improvement in 1-year relative survival not confirmed in 5-year relative survival might indicate aggressive early treatment that did not improve long-term outcomes and in this study we were mainly interested in documenting real gains in AYA survival.

In our database, coverage by country was quite variable. However, we present European survival estimates that are less likely, than country comparisons, to be biased by inadequate representativity of data for some countries.

Two age definitions of AYAs (15–24 years and 15–29 years) are widely used in the scientific literature. We used the age 15–39 years definition proposed by the National Cancer Institute[10] and endorsed by the ENCCA, based on the reasoning that this age category has had relatively little improvement in survival, and a major concern for AYAs with cancer is that they do not have a "home" in research and health care.[10]

In the absence of an updated classification of cancers occurring in AYAs,[31] we used an ad-hoc classification into 46 diagnostic categories based on cancer morphology and site.

A strength of our study was that we evaluated outcomes in a large population-based database of child, AYA, and adult cancer cases archived by European cancer registries. In the future, data provided by these registries will be vital to assess whether changes in management policies have the desired effect to improve survival in European AYAs who develop cancer.

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